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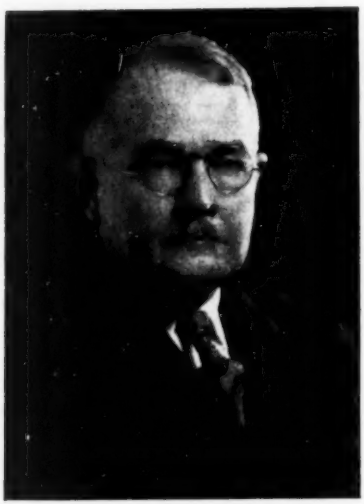

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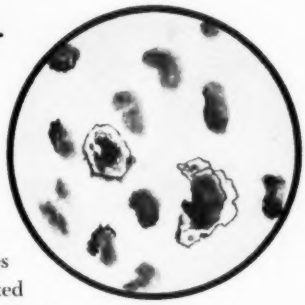

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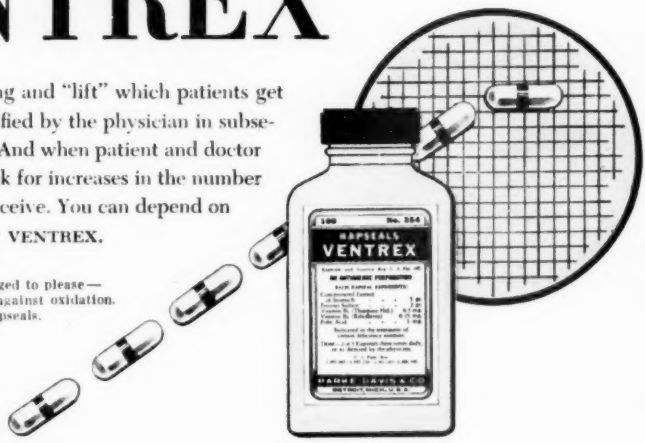

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E D I T O R I A L

INDIVIDUAL RESPONSIBILITY

WITH the dawn of the new year, 1949, one issue, by its magnitude and its all pervasive nature, dwarfs all others into insignificance. It is the real basis of the conflict between East and West, between Church and State, labor and capital and all of the other major conflicts that make living in 1949 far from the happy and peaceful experience that our forefathers may have envisioned it.

To the outward observer it would appear that the world is rapidly drifting toward totalitarianism. Many decry the rapid progress being made by such ideology but few indeed are they who attempt to analyze the basic cause of this phenomenon. Even fewer are they who would be willing to apply *positive* measures for the reversal of this trend. Most of the effort expended is negative; it is directed against something that is considered to be bad rather than for something that is outstandingly good.

The growth of collectivism and its essential corollary, dictatorship, cannot be blamed, as it often is, on the acts of a few evil men. It is due to a breakdown in the moral fiber of the people accompanied by a loss of that feeling of personal responsibility essential in a free, democratic society. To believe otherwise is to argue that the inmates of a penitentiary are restricted and regimented because of the intrinsic evil of their jailers. They are so restricted because no other system will work, they being the individuals that they are. This is exactly the cause for the growth of dictatorships and its growth will not be checked until we as individuals appreciate this fact and make the changes necessary to reverse this trend.

The basic difference between a totalitarian state and a democracy is essentially the difference between a *team* of horses and a football *team*. In the former all depends upon the will and commands of the driver, no decisions are made by the horses themselves. In the latter, the progress of the team depends upon each individual thinking and acting, not with his personal gain as the sole motive, but with the achievement of the team as his primary goal. The trouble today is that too many, who profess to believe in the teamwork that must

underly a democracy, fail to practice it. If in a democratic state any sizable proportion of the individuals think, act and work with only their own advancement in mind, if they do only those things they must and none of the things they should, then democracy begins to fail. More and more encroachment on individual liberty takes place as laws seek to take the place of conscience and good will. The end result, whatever its name, is a society in which the individual is forced by authoritarian police methods to do those things which once were done voluntarily.

In our country, in the last two decades, the people have changed dramatically. The individual workman, today, rarely takes pride in his work; the least that will "get him by" is the rule rather than the exception. Few are motivated by charitable impulse to help the unfortunate. "Let the government do it," is the all too common reply. Many of those in high office are so completely motivated by self interest that their conduct in public affairs is a disgrace. Even some churchmen, who should by their own religious doctrine teach kindness and brotherly love, only too often engage in bitter internecine debate and consider dogma and denomination the things of primary importance. Labor spends much of its time impugning the practices of capital and those responsible for the operation of industry rarely place the happiness and satisfaction of workers on the level it belongs in their planning. No area of our life is without this lack of concern for others, a cancer which slowly but surely is growing in malignancy.

Since the fault is with the individual it must be corrected there. It cannot be done by law, force or argument. We can be regimented by government into a strict pattern of conduct with so called "social legislation" taking the place of cooperation, kindness and philanthropy, but this indeed is not democracy and true Americans revolt at the thought of such substitution. What can be done? Given some great leader, his example and encouragement might turn the tide of events. Such leaders have lived in the past and certain religious faiths presumably follow their teachings. These teachings are still valid, as they shall always be, in guiding the affairs of men. Possibly some day they will become the model for human conduct and followed conscientiously by all people. Unless this happens or some other influence causes the rebirth of a sense of individual responsibility towards one's fellowman, the trend in human events will continue its down-

ward path into regimentation, degradation and the ultimate destruction of all human values. We must in truth learn to love our fellowman in a manner that transcends race, religion and national boundaries. If "Love Thy Neighbor" is taken to mean, as it so often does, only those of the same racial origin, religion and nationality as ourselves, then this precept is but a hollow phrase.

If, in our efforts to combat the growth of collectivism throughout the world, we do not at home make conditions for democracy more favorable, unless we as *individuals* live so as to deserve the fruits of democracy, then we shall fail to achieve it or preserve it at home or abroad and the noble experiment dedicated to the dignity of man shall come to an end. The ultimate decision rests not with those in high office but in the heart of each man and woman everywhere.

L. F. Tice

THE DETERMINATION OF ALDEHYDES*

By Alfred Halpern, Ph. D.**

THE analysis of volatile oils for aldehyde content has long been a problem to the pharmaceutical chemist. Consequently many methods have been suggested, although few have attained practical significance. The more commonly used procedures are:

1) The bisulfite method (1), an absorption process based on the general reaction (I):

I. $$R-CHO + NaHSO_3 \xrightarrow{H_2O} R-\underset{\displaystyle SO_3Na}{\overset{\displaystyle H}{\underset{|}{\overset{|}{C}}}}-OH$$

which forms a water-soluble addition compound, separable from the non-aldehyde portion of the oil and conveniently measured in a graduated *cassia* flask.

2) The neutral sulfite method (2, 3), an absorption procedure according to the following reaction (II). The end-point of the reaction is

II. $$R-CHO + Na_2SO_3 + H_2O \longrightarrow R-\underset{\displaystyle SO_3Na}{\overset{\displaystyle H}{\underset{|}{\overset{|}{C}}}}-OH + NaOH$$

determined by neutralization of the sodium hydroxide against phenolphthalein.

3) The phenylhydrazine method is dependent upon the formation of the phenylhydrazone of the aldehyde, with subsequent titration of the excess phenylhydrazine with standard acid.

III. $$R-CHO + C_6H_5NHNH_2 \longrightarrow R-CH=NHNC_6H_5 + H_2O$$

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* Contribution from the School of Pharmacy, Duquesne University. This investigation was aided by a grant from the Women's Auxiliary of the Allegheny County Retail Druggists' Association, Pittsburgh 19, Pa.

** Assistant Professor, School of Pharmacy, Duquesne University, Pittsburgh 19, Pennsylvania.

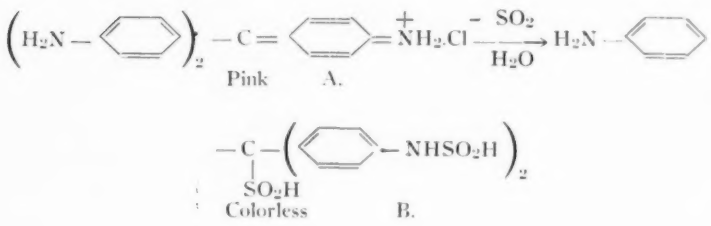
4) The hydroxylamine method similarly utilizes the reaction between the aldehyde and hydroxylamine to form the oxime (IV).

IV. $R-CHO + NH_2OH.HCl \longrightarrow R-CH=NOH + H_2O + HCl$

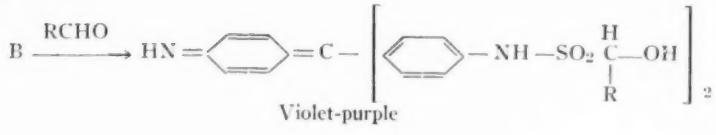
Two related techniques have been developed with this procedure. The first (5) makes use of a solution of the hydroxyl amine hydrochloride and subsequent determination of the liberated hydrochloric acid with standard alkali; the second (6) employs a neutralized solution of the hydroxylamine and after the completion of the reaction the base is titrated with standard acid.

5) The fuchsin-sulfite method (7), based on the development of a color caused by the interaction of the carbonyl group with decolorized fuchsin. Fuchsin, a pink triphenylmethane dye, is converted to the colorless leuco-sulfonic acid by sulfurous acid. On further sulphurous acid treatment it forms the bis-N-aminosulfinic acid which combines with two moles of the aldehyde to produce a complex. The complex then loses sulfurous acid to form a violet quinoid dye. The color developed is compared to a standard and the aldehyde content computed.

V.



VI.



The different methods of analysis have many advantages. However their relative success depends upon many factors and the limitations should be noted.

The absorption methods have several obvious drawbacks. Water-soluble adulterants analyze as apparent aldehydes. The reaction time is an important consideration. There is no control of this factor with the bisulfite method. The completion of the reaction may be determined rather accurately by the use of the phenolphthalein end-point with the neutral sulfite method. The neutral sulfite reaction is in equilibrium and the sodium hydroxide must be neutralized periodically to permit completion. Feinberg (8) found the sulfite method usable only with formaldehyde and benzaldehyde, with not too reliable results in the case of benzaldehyde. He examined several neutral sulfite procedures and pointed out the difficulties in each, all due to equilibrium and end-point. The use of indicators to determine the end-point of the reaction is rendered difficult because of the buffer systems involved which dull the endpoint.

Recently Siggia and Maxcy (9) described an improved procedure for the determination of aldehydes utilizing sulfuric acid to consume the liberated sodium hydroxide, thus forcing the reaction to completion. The excess acid was then titrated with standard alkali. To lessen the difficulties involved in determining the end-point of this titration, a pH meter was used.

The phenylhydrazine method has been largely replaced by the hydroxylamine method. This latter method has few limitations. Foremost among these is the fact that the molecular weight of the aldehydes is the basis for calculation, thus adulteration with low molecular weight aldehydes gives high results. The end-point of the titrations involved is rather difficult to ascertain, especially in the more colored oils (10).

The fuchsin-sulfite method employs rather unstable reagents. The use of freshly-prepared standards makes the procedure rather lengthy although a high measure of accuracy is achieved by an experienced analyst.

In view of the above difficulties in the determination of aldehydes, it was deemed important to apply the techniques described by Siggia and Maxcy (9) to the determination of aldehydes in pharmaceutically-important preparations. As a secondary phase of

this study, the use of a pH titration curve for the determination of aldehydes by the hydroxylamine method was investigated.

Experimental

The physical properties of the oils and aldehydes used in this study are reported in Table I.

TABLE I

The Physical Properties of the Aldehydes and Volatile Oils.

Aldehyde/Oil	B.p.°	D20/20	η_d^{20}
Acetaldehyde	21	———	1.3317
Anisaldehyde	247	———	1.5768
Benzaldehyde	179	———	1.5456
Citral	228 dec.	———	1.4875
Citronellal	206	———	1.4681
Cinnamaldehyde	253	———	1.6195
Decylaldehyde	208	———	———
Phenylacetaldehyde	194	———	1.5255
Salicylaldehyde	196	———	1.5735
Bitter Almond Oil	——	1.050	1.543
Cassia Oil	——	1.060	1.603
Cinnamon Bark Oil	——	1.012	1.572
Citronella Oil (Ceylon)	——	0.903	1.482
Cummin Oil	——	0.915	1.503
Lemon Oil	——	0.858	1.474
Lemongrass Oil	——	0.901	1.486
Orange Oil (Bitter)	——	0.854	1.473

The pH of the end-point as determined by Siggia and Maxcy varies with the aldehyde used. Since they reported values for a limited number of aldehydes, their procedure was repeated using other aldehydes in order to obtain the end-point constants. The pH of the solutions at varying levels of the titration was determined with the Fisher Titrimeter and the Hellige pH meter. A graph was constructed plotting mls. of 1 N sodium hydroxide *vs.* pH. The end-points were derived from the graph. (Table II) Since the curves for the aldehydes are nearly identical, a representative curve for the aldehydes studied is reproduced in Figure 1.

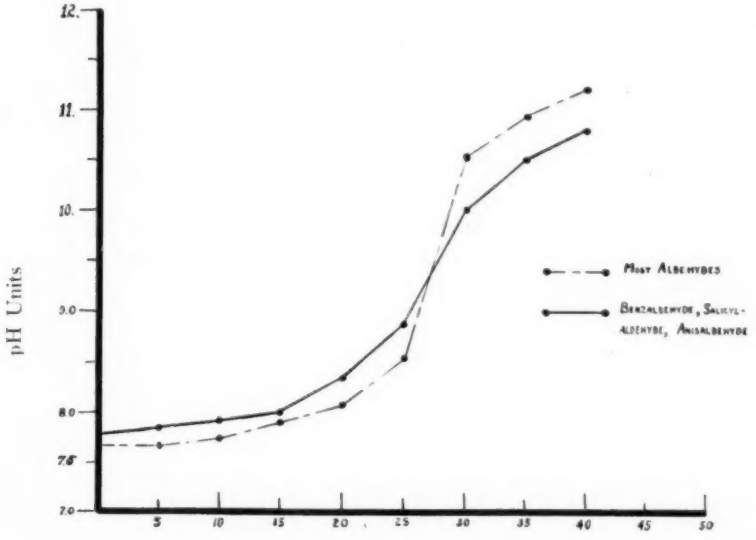
TABLE II

Observed pH at the End-Point of the Siggia-Maxcy Method.

Compound	pH Range	Sample Taken Mole x 10^{-2}(a)	Observed Mole x 10^{-2}(b)
Acetaldehyde	9.00—9.10	2.31	2.28±0.02
Anisaldehyde	8.7 —8.9	2.56	2.54±0.05
Benzaldehyde	8.85—9.0	3.10	3.24±0.12
Cinnamaldehyde	9.5 —9.6	3.17	3.20±0.02
Citral	9.2 —9.3	2.64	2.64±0.03
Citronellal	9.3 —9.4	2.27	2.93±0.16
Decylaldehyde	9.6 —9.7	2.46	2.45±0.02
Phenylacetaldehyde	9.15—9.25	3.16	3.08±0.09
Salicylaldehyde	8.83—9.0	2.83	2.73±0.19

(a) A stock solution was prepared so that the indicated molar concentration was present in 5 ml. of 95 per cent ethanol solution.

(b) These values represent the mean of six determinations with the mean deviation.



Mls. of 1N Sodium Hydroxide

TYPICAL TITRATION CURVES FOR THE ALDEHYDES

FIG. 1

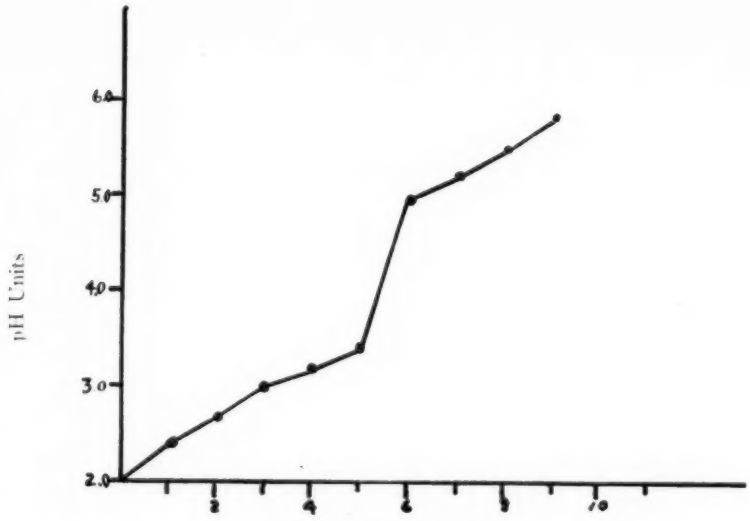
The Siggia-Maxcy Method (9): Fifty mls. of a N sulfuric acid solution are added to 250 mls. of a 1 molar sodium sulfite solution in a 500 ml. glass-stoppered erlenmeyer flask. To this solution is added the sample to be tested containing 0.02 to 0.04 moles of the aldehyde. The flask is stoppered and shaken for 2 to 5 minutes to insure complete reaction. The contents are then quantitatively transferred to a beaker. The electrodes from a pH meter are then inserted into the solution and the solution is stirred. The pH of the solution is noted, as standard 1 N alkali is added to titrate the excess acid. The pH *vs.* mls. of alkali added is plotted and the end-point determined from the plot. A more rapid method of determining the end-point (though less precise) is to add alkali until the pH is obtained which corresponds to the pH for the particular aldehyde. Since sodium sulfite contains a small amount of alkali as an impurity, a blank is run. The amount of alkali present in 250 mls. of sodium sulfite solution consumes about 0.4 to 0.5 ml. of acid. It is suggested (9) that enough 1 M sodium bisulfite be added to neutralize the free alkali and bring the pH of the sulfite solution to 9.1.

The hydroxylamine method of the U. S. P. XII (5) was applied to the aldehydes and the pH of the titration at varying levels was determined by the Fisher Titrimeter and the Hellige pH meter. The end-point was determined from a plot of the pH values *vs.* mls. of NaOH. There was very little difference (about ± 0.03 pH units) among the values obtained with the different aldehydes. The curve of the mean values is reproduced in Figure 2.

In order to better evaluate the various methods, a comparison of the total aldehyde content was made using the pure aldehyde and the whole oil.

Discussion

The different methods of analysis gave a fair degree of agreement. It is obvious from the data presented in Tables III and IV that no general method is applicable to all of the aldehydes. The use of a potentiometric end-point greatly facilitates the hydroxylamine and the neutral sulfite methods. Since the whole oils are mixtures with varying composition it is important to determine the end-point prior to the unknown determination with the Siggia-Maxcy method. Once this value is obtained, the control analyses can then be determined using this specific value. Using the whole oil obtained from



TYPICAL CURVE OF TITRATION OF ALDEHYDES
IN THE HYDROXYLAMINE METHOD
FIG. 2

two different manufacturers, a variation of .03-.15 pH units from the value of the isolated aldehyde was obtained.

It was noted by Siggia-Maxcy that their method was not applicable to ketones. Their conclusion is well in accord with our experiences using pulegone, carvone and menthone.

The potentiometric end-point determined for the hydroxylamine method is after the development of the full yellow color using methyl orange as the indicator, thus explaining a possible source of error in the determination. The pH of the derived end-point is 4.42; methyl orange develops the full yellow color after a pH of 4.2, bromphenol blue has its stable color change at a pH of 4.5 which might explain its advantages in this determination (11). Dimethyl yellow, developing its full color at a pH of 4.6 is a preferred indicator. It should be remembered that the other constituents of the whole oil may interfere with the color development. This limitation is not present in an end-point derived from the titration curve.

Since non-concordant values for the endpoint were obtained with some ketones, this phase of the study is still under investigation and will be reported at a later date.

TABLE III

A Comparison of the Methods of Analysis for Aldehydes

Compound	Sample Size Mole × 10^{-2}	Bisulfite Absorption (a)	Found — Moles × 10^{-2} Neutral Sulfite (b)	Siggia-Maxcy (c)	Hydroxylamine Indic. (d)	Hydroxylamine pH (e)	Fuchsin Sulfite (f)
Acetaldehyde	2.31	———	2.30 ± 0.04	2.28 ± 0.02	2.30 ± 0.06	2.29 ± 0.04	2.31 ± 0.02
Anisaldehyde	2.56	———	2.53 ± 0.13	2.54 ± 0.05	2.56 ± 0.04	2.55 ± 0.02	2.54 ± 0.12
Benzaldehyde	3.10	———	3.14 ± 0.06	3.24 ± 0.12	3.04 ± 0.12	3.09 ± 0.03	3.14 ± 0.03
Cinnamaldehyde	3.17	———	2.91 ± 0.12	3.20 ± 0.05	3.19 ± 0.11	3.19 ± 0.02	3.14 ± 0.06
Citral	2.64	———	2.31 ± 0.14	2.64 ± 0.03	2.53 ± 0.16	2.60 ± 0.06	2.56 ± 0.13
Citronellal	3.27	———	3.00 ± 0.15	2.93 ± 0.16	3.16 ± 0.17 (g)	3.28 ± 0.05	3.21 ± 0.08
Decylaldehyde	2.46	———	2.38 ± 0.10	2.45 ± 0.02	2.48 ± 0.04	2.45 ± 0.03	2.47 ± 0.04
Phenylacetaldehyde	3.16	———	3.12 ± 0.06	3.08 ± 0.09	3.15 ± 0.08	3.11 ± 0.03	3.08 ± 0.08
Salicylaldehyde	2.83	———	2.91 ± 0.24	2.73 ± 0.19	2.91 ± 0.18	2.88 ± 0.09	2.79 ± 0.17

a) The aldehyde was completely soluble in an excess of the bisulfite.

b) According to the procedure described in the U. S. P. XIII, page 132.

c) Values taken from Table II.

d) According to the procedure described in the N. F. VIII, page 31.

e) Using the end-point derived from figure II.

f) Methods of Analysis, A. O. A. C., 5th Ed. (1940) page 324.

g) According to the modification proposed in the Analyst, *57*:773 (1932).

TABLE IV

TOTAL ALDEHYDE CONTENT OF THE VOLATILE OILS BY THE DIFFERENT METHODS

Oil	Sample Grams	Found—Per Cent: Bisulfite Absorption (a)	Neutral Sulfite (b)	Siggia-Maxcy (c)	Hydroxylamine Method: Indicator (d)	Hydroxylamine Method: pH (e)	Fuchsin Sulfite (f)
Bitter Almond Oil	0.6541	88.3	87.9	87.1	85.4	85.7	86.0
Cassia Oil	0.8736	84.7	85.0	84.9	81.2	82.4	82.1
Cinnamon Bark Oil	1.0713	62.5	61.3	61.5	60.9	61.2	62.2
Citronella Oil, (Ceylon)	1.0035	8.8	8.6	8.7	8.6 (g)	8.6	8.6
Cummin Oil	1.1264	39.2	39.1	—— (h)	38.5	38.7	38.7
Lemon Oil	1.2163	4.8	4.7	4.5	4.5	4.5	4.6
Lemongrass Oil	1.1215	79.2	81.4	80.93	79.21	79.34	79.5
Orange Oil (Bitter)	7.6510	1.1	1.2	1.1	1.1	1.1	1.1

a) According to the procedure described by Garratt, (Reference 1).

b) According to the procedure described by the U. S. P. XIII, page 132.

c) Using the end-point derived from Table II.

d) According to the procedure described by the N. F. VIII, page 31.

e) Using the end-point derived from figure II.

f) According to the procedure described by the Official Methods of Analysis of the A. O. A. C., 5th Ed. (1940), page 324.

g) According to the modification described in the Analyst *57*:773 (1932).

h) Cummin aldehyde was not available for the determination of the end-point by this method.

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GOVERNMENT MEDICINE IN NEW ZEALAND—ITS SOCIAL, ECONOMIC, AND POLITICAL IMPLICATIONS *

By A. Lexington Jones, D. D. S., M. S.**

PERHAPS before considering the main subject of my address it may be pertinent to give you a thumb-nail sketch of New Zealand—it will give some background and enable you to appreciate more fully what has to follow—a clearer picture from which to evaluate the economic and medical features.

The Dominion of New Zealand consists of an isolated group of islands, two of which are comparatively large. This group is situated approximately 1200 miles east of Australia, 6000 miles west of South America and 1600 miles North of the Antarctic Continent. The principal islands lie approximately between the parallels of 34 degrees and 48 degrees south latitude and the meridians of 166 degrees to 179 degrees east longitude. The total area including annexed islands is 103,935 square miles.

The dominion has a climate of marine type—not excessively hot in the summer and not unpleasantly cold in the winter. Most parts of the country enjoy ample rainfall and a liberal share of sunshine. The mean daily temperature (Fahrenheit) is about 44 degrees to 64 degrees. This is an average taken over many years.

New Zealand has been described by some people as the socialistic laboratory of the world—this may or may not be true. At least one other country in the world—a much larger one and with a greater population claims this distinction. The methods adopted in the implementation of the Socialist regime may be different, but the principle underlying that order of life is the same.

The socialization of medicine in New Zealand was completed in 1938 and became operative on April 1, 1939. The principal objects of the Social Security legislation are as follows:

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1—To substitute for the system of non-contributory civil pensions, for example old age pensions, widows and other pensions, a system of monetary benefits on a contributory basis.

2—The inauguration of a system of medical and hospital benefits and other related benefits, e. g., pharamaceutical, dental, masseur, etc.

It is section No. 2 that I am to discuss today—but section No. 1 requires some elaboration so that you may judge whether or not the latter was desirable or necessary.

The system under which we operated, pre-1938, was in effect much the same as the one at present existing in America today. Provision was made for the aged, infirm and sick to secure state assistance in the form of pensions and free hospital treatment where necessary. This system was augmented by means of benefit lodges, insurance companies and other private means of providing self security in time of need. Such private schemes became inoperable after the introduction of "Social Security" as sponsored by the Government and in effect became impracticable and have almost gone out of existence. The introduction of the government scheme compelled everybody in New Zealand to come within its scope and the payment for this stupendous undertaking was provided for by means of direct taxation. The net income of everybody in New Zealand is taxed 23¢ (one shilling being approximately 20 cents). This tax is calculated on the first dollar of income and no exemptions are allowed. You will note that 5½¢ out of every dollar of income or salary is collected as a special tax. This amount only partly covers the cost of administration of Social Security. In addition the fund must be subsidized from the Consolidated Fund of Government. The taxation revenue of general government fund in 1945-46 was $460,000,000, an amount equaling $268 per head of the population. In that same year the expenditure on Social Security alone was $104,000,000—equaling a sum of $60 per head of population. Nearly ¼ of the government income was expended on the social security program. I present these figures to you so you may acquire a right persepective of the cost to each individual in our country and dispose of any ideas that the benefits of socialization of medicine and related professions is free to any fellow citizen. Can any economic system stand up to such an overload of taxation?

Let us now consider the administration of this socialistic scheme. Medical, dental and pharmaceutical practices are operated much in the same way as in this country. Similarly does the hospital system resemble that adopted here. We have our state controlled and privately owned institutions to which any person is entitled to be admitted, if there is available accommodation. Under the Amended Social Security Act, which came into operation on November 1, 1941 "every person is entitled, without cost to himself (note without cost) to such medical attention (with certain specified exceptions) as is ordinarily given by medical practitioners in the course of general practice. The medical practitioner is entitled to receive the sum of $1.50 for every time he renders any of the prescribed services. If the practitioner is called upon to provide, in response to an urgent request, services on a Sunday or between the hours of 9:00 P. M. and 7:00 A. M. the appropriate fee is increased to $2.50. Mileage fees are also payable in certain circumstances. Any charges over and above the fees quoted are payable by the patient."

Gentlemen, that is a copy of the section of the act. Pharmaceutical benefits are provided "free of any cost to the patient"; state hospital benefits are provided free of cost to the patient; private hospital charges are subsidized up to $2.00 per day during period of hospitalization; maternity benefits are free in state hospitals and subsidized in private hospitals and private practitioner's fees are in accordance with a prescribed scale and are to be regarded as full settlement of his claim. In case of specialists, additional fees over basic allowances must be recovered from the patient.

Besides these benefits we have Monetary Benefits listed under child benefits ($2.00 per week per child under 18 years.).

Superannuation benefits of $40.00 to a maximum of $416.00 per annum is provided. We have also old age, widows, orphans, invalid, miners, Maori war, unemployment, sickness, emergency, dental, laboratory, nursing, massage, and X-ray diagnostic service in addition. The chiropractors are now making representation for their inclusion. Additional to these we have our war pension, economic pensions, war veterans allowance, emergency reserve corps pension and Mercantile Marine pensions. Truly a scheme to care for New Zealanders from the womb to the tomb.

Let us now consider the practical application of the foregoing with regard to the medical practitioner. Please bear in mind the

quoted phrase "without cost to himself." A patient visits his doctor. At the conclusion of his consultation he signs a form. That form is signed by the doctor and directed to the health department for whatever sum involved, a minimum of $1.50 per visit. The form is a simple one. The doctor's name appears on it, the number of visits the patient has made and the total cost. The claim is then signed by the doctor and paid without query or question.

The patient is free to visit as many doctors as he wishes per day, per week or per year "without cost" to himself at the time of the visit. He may obtain from each doctor a prescription which he may have filled without cost to himself. He may be signed over to any one of the subsidiary benefits for a pension, admission to a hospital, massage, X-ray and so on. He may indulge in this peregrinating pastime among the doctors till his heart is content or until he finally interviews a doctor who will do as he bids, give him the medicine he desires and put him in the institution of his choice and place him on the advantageous "pension list." This he may do without cost to himself. The one and only condition is that he be prepared to wait in a queue of people on similar business bent. He may even be ill and in need of urgent attention, but he will of necessity have to join the endless chain of the sick and the imaginary sick. All of this he is legally allowed to do and all of these charges he is permitted to incur by the law of the land, the Social Security Amendment Act of November 1941. I have presented you with facts only as published in the Abstract of Statistics of 1947.

The interpretation of the act is the one in force and duly exercised. The number of indoor patients treated in public hospitals in 1945 was 165,000. We may assume that another 40,000 were treated in private institutions, making a grand total of 206,000 or 12½% of our total population under hospital care, a startling figure for a country the size of New Zealand. Based on this figure America would have to provide accommodation for 17,000,000 as a permanent hospital population.

Nobody will deny the sick of any country the right to adequate treatment, but the cost to the country is tremendous, not because the money is being spent on the individual but because of the immense cost of administration and the abuse of the system under a socialist government. Some of these abuses I will refer to as I go along.

The questions we ask ourselves in New Zealand are:

1. Are we getting our money's worth?
2. Has the system improved medical service to the people?
3. Has the system reduced the incidence of disease?

To question one I reply, most certainly not. A great part of the money we are taxed is absorbed in the cost of administration—in the payment of a large body of civil servants and for the payment of doctors for visits that were never necessary and for prescriptions given them.

To question two, I again say no. The medical profession has so many consultations that it is impossible for them to devote the necessary time to each patient, evaluate their symptoms and give a careful and considered diagnosis. I do not say this in any derogative way regarding the members of the profession. It is not humanly possible. Too many are consulting their physician unnecessarily, taking up his time which would be better given to people really needing his attention.

Regarding question three, the figures speak for themselves. A very small amount of money is voted for research work. The physicians have little or no time for reading and investigation, and little incentive to study abroad.

The system as operated in New Zealand allowed itself of such abuse that it has almost become a farce and I have listed a number of questions that I feel are in the minds of you present.

1. Are medical services available at no cost to the patient? *My answer.* Of course not, the average cost to each individual is $60 per annum. To many it is not this high, but to many more a great deal higher.
2. Has it raised the status of medical profession? *My answer.* No. It has lowered their prestige due to known abuses that may be practised by unscrupulous members.
3. Is it possible for unscrupulous members to be dishonest? *My answer.* Blatantly so. A form could be filled in for more visits than the patient paid to the doctors, a signature could be forged, forms could be filled in by friends of the doctor when no visits were made.

4. Can the pharmaceutical benefits be made available wrongfully? *My answer.* Yes, as of the right any prescription signed by a B. M. A. member must be filled by the chemist without questions.

5. Is there any competent check made of medical claims? *My answer.* No. They are checked by departmental clerks whose duty, in the main, is to compute the amount for direction to the treasury for a check to be paid out to the doctor each month.

6. Is socialized medicine less costly to the patient than other schemes? *My answer.* The average cost per head is $60.00, but many people pay much more. In a very small minority this scheme may save money. To the great masses it is far too high. In 1941 medical schemes took care of people unable to meet medical fees.

7. Was the socialization of medicine the first profession to be brought within the orbit of state control? *My answer.* Such a step is embodied in the prepared plan for all communistic activities. Lenin said, "Socialized medicine is the keystone to the arch of the socialist state." In New Zealand they have been true to form.

8. Do you consider there is much waste of money in the administration of the scheme? *My answer.* Yes. An army of civil servants are engaged full time in routine office work, checking claims, etc., for all benefits under the scheme. In 1940 much of this work was done voluntarily by lodge members or by secretaries to lodges and to doctors. Most doctors have found it necessary to engage a full time secretary whose work is to have forms signed and checked, etc.

Pharmaceutical benefits are particularly abused, because it costs the patients nothing. They do not use all that has been prescribed or they use much more than necessary. Many of the homes in New Zealand could discover a dozen or so bottles of medicine only half empty. There is an old saying, "Anything acquired for nothing is worth nothing." I fear the people in New Zealand have that attitude to their free medicine.

9. Do you think the economic structure of New Zealand can stand up to this tremendous change? *My answer.* I think the day of reckoning must come. It is the great waste of money and time that will bring ruin to the scheme.

10. Did the people of New Zealand oppose the introduction of the scheme? *My answer.* Yes, a small section, the B. M. A. They were very vocal in opposition, but they were not supported by the business community. The people in New Zealand failed to realize that this was the socialist technique and did not appreciate the effect it would have on their lives. It was their apathy in opposing the Socialists that made passage of our law possible. They were hoodwinked by promises of something for nothing. It was the "thinking" people of my country who did not register their opposition. They are the people in this country upon whom must be impressed that the price of security is their freedom.

11. Do you think that the incentive for post graduate work has been removed? *My answer.* Yes. Members of the profession feel that any higher qualifications or advanced study is discouraged. Such a course is expensive and probably not recoverable from the public.

12. Has it had any effect on the relationship between the doctor and the patient? *My answer.* Most certainly. That confidence, so necessary, has been lessened because the dignity and prestige of the profession has suffered.

Having thus far dealt with the actual socialization of medicine in my country, its cost to the people, its objective, its apparent good and its apparent evil, may I now address to you some remarks, bearing upon the impact on society which socialization has had.

These views are my own but they are shared, I am bold enough to say, by the majority of New Zealanders.

Since 1941 the New Zealand Government has brought under its power, The Bank of New Zealand, the dental profession, chemists, masseurs, National Airways, etc. This procedure merely goes to prove that the regimentation of the medical profession was the forerunner of a carefully calculated procedure as outlined by those fellow travellers, the communists. And here I sound a note of warning—

take heed America lest it happen here. Don't say it cannot. New Zealand said it and so did every country that today is under the heel of dictatorship. *It can and it will,* unless you band yourselves together in a national forum and oppose it with all the strength you can muster. Passive resistance, subdued mumblings of disapproval among yourselves will get you nowhere. The people of this great country must be informed of the danger that stalks them, all sections must be made aware of the subtle methods adopted by the exponents of socialism. They must be made aware of the inevitable developments if such a system is countenanced in this fair land. The people must be warned of the honeyed words of its advocates, the sly and camouflaged propaganda, the fallacy of the plan of "Utopia in our time" and the "something for nothing" theorists. They must be convinced that in the realm of politics, sociology and economics the layman is very liable to accept bad practices if they are adroitly concealed with good intentions. Every collectivist argument involves the "welfare" of the people and such specious statements are misleading and misguided. There is no important difference between the collectivist systems, be it socialism, communism, nazism or fascism. In the end they all reduce the citizen to the position of abject submission to cruel and capricious bureaucrats, a condition which adherents to this collectivist system seem to condone. Adherents and advocates of a system which subjugates the rights of the individual to the state have a "Modus operandi" so to speak. It is a constant equation. It never changes. They advance upon society and incorporate it in the state—piecemeal—cell by cell. In this manner they never raise the voice of objection of the masses of the people at once and so avoid concerted opposition. Like Hitler, "We have no further territorial ambitions", till all is quiet and the stage set again for, "peaceful penetration." I do not propose delivering a diatribe on the strategy of socialism. I merely mention these points because in New Zealand I experienced this form of collectivist strategy. The majority of the inhabitants of my country failed to appreciate the end result and refused to heed the warning given, refused the hear the word of reason, and as a result socialism took the helm.

I am a father of seven children and it is my duty and my pleasure to provide them with food, clothing and shelter, and by precept and example make them good citizens. I wish to see them develop the attributes of courage, initiative, enterprise, self reliance

and good Christian characters. Is it possible under a socialist dominated country where the only avenue of employment will be with that of a soulless state, a mere automaton, a cog in the vast machinery of collectivism?

In my opinion socialism encourages indolence, it disapproves of the development of individualism or self reliance, it strikes at the very moral fibre of our young people and destroys the fabric of their character. I do not wish to see my family grow up unaware of the dignity of work and devoid of the sense of pride of achievement. I wish them to have to work and shape their own destinies, to learn of the value of adversity and enjoy the sweet fruits of success gained for themselves and by their own effort.

I do not wish them to grow up the dupes of arrogant and calculating wreckers whose ambition will be realized only when Communism becomes a reality and then the opportunities of their country, this world and their lives have been frittered away. Then it will be too late to save themselves for the final reason that there will be nothing to save. That is why I suggest that all Christian people should band themselves together and form that National Forum and face up frankly and brutally to the question, "Are we going to stand it any longer?"

There is no hysteria about this. I am speaking from experience. I am speaking as a lover of freedom who sees liberty being filched from me by impractical ideologists who have become fanatics.

The world today is one vast seething mass of discontent, suspicion, unhappiness and uncertainty. We have just concluded a war against German National Socialism, the most bloody war the world has ever known. Six long years of bestial brutality. We witnessed the cities of Europe being bombed and blasted and burnt. Tens of thousands of our best moral men and women laid down their lives on the battlefields and in the cities of war torn Europe and the Pacific, thousands of little children were killed, thousands of others died of disease and starvation—all to halt the Nazi hordes. The cost in human life and misery was great—all this to stem the tide of dictatorship. Today we face the possibilities of yet another brutal war. This time, against another country, but against a similar enemy and for the same reason, to preserve our way of life, our freedom and liberty. I see in the socialization of medicine the first stage of the encroachment upon our civil liberties and we must convince all of our

people that their freedom is undoubtedly tied up with every other section of the country.

The greatest tyranny has the smallest beginnings. From precedents overlooked, from remonstrances despised, from grievances treated with ridicule, from powerless men oppressed with impunity, and overbearing men tolerated with complacence, springs the tyrannical usage which generations of wise men may later perceive, lament and resist in vain. At present, common minds no more see a crushing tyranny in a trivial unfairness or a ludicrous indignity than the eye, uninformed by reason, can discern the oak in the acorn or the utter desolation of winter in the first autumnal fall. Hence the necessity of denouncing with tireless perseverance every single act of oppression. Let it alone and it stands on record. If the country has allowed it and when it is at last provoked to indignation and resistance it finds itself gagged with the record of its own inertia.

Socialists are flying in the face of the natural law. This law cannot be shouted down by mobs, nor argued out of existence by doctrinaires or repealed by governments. It has stood the test of time and around it has developed our society as we know it now. In effect, socialism seeks to take away someone's rights to which, under custom and belief of the people, he is rightly entitled. I have said that socialism strikes at the very roots of democracy. Karl Marx wrote "The democratic concept of man is false because it is Christian. It holds that each man has a value as a sovereign being. This is the illusion, dream and postulate of Christianity."

Hitler wrote, "To the Christian doctrine of the infinite significance of the individual's human soul, I oppose with icy clarity the saving doctrine of the nothingness and insignificance of the individual human being."

Under these two isms God can have no place in the totalitarian state. In his place stands the Dictator. Our civilization is based on Christianity.

I appeal to you to be up and doing. In the unchangeable pattern of socialism you are to be the next victim. Should you submit—then you permit the laying of the foundation for a totalitarian structure to be built. If you allow totalitarianism to exist here on any scale, then you expect it to be maintained by gestapo police methods—dictatorship, loss of liberty and opportunity and resultant degradation of the mass of people.

In conclusion, I hope nobody says "I have enjoyed your speech." I have not given it for your enjoyment. I hope it worries you excessively. I hope it causes you sleepless nights until you have done something about it, until you join the national forum. I hope your action will be affirmative and effective so that you will safeguard your rights of democracy—your way of life—the American way of life.

Wendell Willkie once said, "This program will not interest those people who regard America as a socialistic laboratory. It will not interest those people who regard this country as a free lunch counter. It will certainly not interest those people who imagine this country as somewhat of a worked out gold mine out of which they wish to snatch a nugget or two for themselves. It will only interest those people who know and love their land—who know that its prosperity was only built up by the thrift and industry of its people and whose greatness can be retained in no other way."

Thank you very much. I wish you much worry and real concern.

THROMBOPLASTIC ACTION OF SOME GALENICAL PREPARATIONS

By David I. Macht,* M. D., Phar. D., Litt. D., F. A. C. P.

COAGULATION of the blood is one of the marvels of creation. If blood did not possess this quality, injuries to the body would allow it to leak out as freely as water leaks through a sieve. This fact which is known to every physician has dominated medical thinking about coagulation of the blood for many years so that great efforts were made by those medical men interested in the subject to discover something which would hasten blood clotting more quickly and thus prevent the dire consequences of hemorrhages following poor clotting of the blood. It is quite clear now, however, that the thoughts of the medical profession must be directed in the reverse direction and we are beginning to realize that under certain circumstances great benefits to health and life can come through impairing the coagulation time of blood and making it longer. The reason for this is because physicians have discovered that *intravascular clotting* of the blood with the consequent thrombosis is a greater danger to life and health than the problems of checking hemorrhage. This fact has been brought into sharper focus by the present writer's discoveries in the last five years concerning the action of certain drugs. It was learned by him while engaged in the study of the anticoagulant drug, heparin, that certain well-known drugs, namely: digitalis and the related digitaloid glucosides such as strophanthin, ouabain, convallamarin, and others exert a thromboplastic influence on whole blood of animals. This finding at first regarded skeptically by some physicians has been largely corroborated and is accepted by most medical scientists at the present time (1-11). Following this discovery, another group of drugs widely employed in medical practice, namely the mercurial diuretics (12, 13), were also found by Macht to exert a definite thromboplastic effect on the whole blood of animals; and perhaps more surprising still was the discovery, first by Moldavsky and his coworkers (14) and later by Macht, (15, 16) that penicillin produces a marked thromboplastic effect both in animals and in human beings. These findings have made medical men

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so to say "coagulation-minded" and the present writer actually predicted when addressing a joint session of the American Therapeutic Society and the Southern Medical Association in Cincinnati, November 15, 1943, that he expected to find other drugs which would show thromboplastic properties when studied by pharmacological and physiological methods.

In the present paper, the author wishes to report briefly a study which was suggested by a passage in Shakespeare's "Hamlet." In Act 1, Scene 5, Lines 68 to 70, we read:

> "And with a sudden vigour it doth posset
> And curd, like eager droppings into milk,
> The thin and wholesome blood: so did it mine;"

Because it has been recently discovered that some commonly employed drugs may possess a thromboplastic property, the author thought it worth-while to examine a number of galenical drugs for their coagulating properties on blood.

Those which were chosen comprised a number of drugs known to physicians of Shakespeare's time, (17) such as hyoscyamus niger, *atropa belladonna*, hemlock, and aconite or monkshood. The results obtained in these experiments were most interesting and are here reported.

Coagulation was at first studied on shed blood in special flat-bottomed homeopathic vials 1.2 cm. in diameter. The method employed was that of Howell or, as it is now better known, the Lee and White Method. One or two cc. of fresh blood is introduced into a series of vials and the time required for coagulation is measured with a stop watch, the criterion being the complete inversion of the vials without a flow of the blood. The various preparations which were studied were examined first in vitro. A small quantity, 0.1 to 0.25 cc. of the galenical tincture was placed in the vial and allowed to evaporate at room temperature. After complete drying the same volume of physiological sodium chloride solution was introduced into the tube and the residue rubbed up with a glass rod. In this way, a series of vials was prepared, some containing control sodium chloride alone and the others the evaporated galenical preparations to be studied. Blood was obtained from rabbits and cats and also from human volunteers and the coagulation was studied as described above.

In the second series of experiments rabbits and cats were injected with diluted solutions of the galenical preparations, the dilution being such as to contain not more than 5 per cent concentrations of alcohol. These suspensions or solutions were injected in some cases intravenously and in other cases parenterally. The coagulation of the blood in each case was first measured before administering the drugs and afterwards at various intervals after injection of the medicaments.

In a third group, and perhaps the most important of experiments, all of the drugs were administered through a stomach tube and blood coagulation before and after administration of the drugs was studied by the Lee and White method.

The phenomenon of blood coagulation has been the subject of intensive and extensive studies for many years and the exact mechanism of coagulation is as yet not completely known although most physiologists agree on the principal factors involved in this phenomenon. To analyze fully the effect of any given pharmacological agent or chemical on blood coagulation would require a study of its effect on (*1*) fibrinogen, (*2*) blood calcium, (*3*) prothrombin, (*4*) anti-prothrombin, (*5*) various thromboplastic elements, such as blood platelets, (*6*) vitamin K, (*7*) certain new factors such as acceleration globulin, anti-hemophilic globulin, Owren's factor V, etc., and various other factors isolated and studied by distinguished physiologists and biochemists (18). For practical clinical purposes, however, the physician is interested primarily in what happens to the whole blood inside and outside the body. For this reason, the author preferred to make his studies on coagulation by the original Howell or Lee and White method, deferring a more detailed analysis of the coagulation mechanism for later research.

Results

The results obtained are clearly exhibited by the subjoined tables. In Table I is listed a series of drugs for the most part official tinctures studied by the author by the methods outlined above, and in the same table is indicated what effect if any is exerted by these on blood coagulation. In Table II are shown the results obtained with rabbits' blood mixed with small quantities of the drugs *in vitro* as described above. Table III illustrates the results obtained

in similar experiments with whole blood from cats. Table IV shows similar experiments performed with human blood. It will be noted that in all of the experiments *in vitro* the results obtained from rabbits, cats and human beings largely agree with each other. In Table V are shown results obtained with injections of diluted tinctures into a rabbit's vein, and in Table VI are a series of illustrative experiments which show the results obtained with various galenic preparations diluted with water and introduced through a stomach tube. Curiously enough, Tincture of Arnica was found to prolong coagulation time in vitro. This, however, did not occur when the drug was injected into rabbits or administered by stomach.

Discussion

It will be noted that several of the well known old drugs, namely those belonging to the belladonna family such as hyoscyamus and belladonna itself, produced a marked shortening of whole blood coagulation time. Tincture of Aconite also was markedly thromboplastic by all routes of administration. Perhaps even of greater interest than hyoscyamus and belladonna were the findings made with opium. Both the camphorated tincture of opium, or paregoric, and the official, stronger opium tincture, or laudanum, in every experiment produced a thromboplastic effect. This finding was of such an interest that a separate study is being conducted not only on opium itself but on various alkaloids and morphine substitutes in regard to their thromboplastic properties. In addition to the galenic preparations mentioned in Table I, several of the alkaloids were also studied and more particularly, hyoscyamine, scopolamine, coniine, morphine and gelsemine. The results obtained with these are shown in Table VII.

In order to obviate any errors in connection with studies on coagulation, numerous control experiments were made and it must be stated that considerable practice is required in drawing blood specimens so as not to introduce errors due to a mixture of various body juices, etc. In order to establish the fact that repeated drawing of the blood either from direct cardiac puncture or from an artery is not conducive to shortening of the clotting time through the operation itself, control experiments of the type exhibited in Table VIII were also performed. In such experiments the normal

coagulation time was studied first, repeatedly, without introduction of any drug. After several such normal tests the drug was administered by stomach tube and coagulation time was studied again, not only on the same day but on the following day. These experiments proved conclusively that the shortening in coagulation time was due to the drug and not to the repeated removals of blood samples.

It appears therefore that Shakespeare's description in Hamlet, Act I, Scene 5, Lines 68-70 was not catachrestic but inadvertently and yet surprisingly correct. A number of galenic preparations have been found experimentally to hasten blood coagulation and among these are hyoscyamus or henbane, belladonna, and conium or hemlock, all of which have been suggested as the drugs described by the dramatist under the name of "hebenon." From the physiological and the clinical standpoint, however, the present study is not only of historical and literary interest but is impressive because of the remarkable provisions of nature which in some hitherto unknown manner protect animals and human beings from succumbing to extreme changes in coagulation time and allow them to survive in spite of many a dangerous medication to which they are subjected. One can well recall with great appreciation the words of the ancient poet, "I am fearfully yet wonderfully made," Psalm 139:14.

Summary

1. A series of tinctures and fluid extracts was studied in respect to their influence on coagulation of whole blood *in vitro* and *in vivo*.

2. Some of these were found to be definitely thromboplastic while others exerted no effect on blood coagulation.

3. Of special interest were the findings made with hyoscyamus, belladonna, aconite, conium, and opium.

4. These findings were of sufficient importance to prompt the author to further investigation of the subject, especially in respect to the action of various alkaloids on blood coagulation.

TABLE I

LIST OF DRUGS EXAMINED

Tinctura	*Coagulation time*
Digitalis	Decreased
Strophanthi	Decreased
Opii	Decreased
Opii Camphoratae	Slightly decreased
Arnicae	Prolonged (*in vitro*)
Nucis Vomicae	No change
Aconiti	Decreased
Cinchonae Comp.	No change
Lobeliae	No change
Hyoscyami	Decreased
Belladonnae	Decreased
Stramonii	Slightly decreased
Valerianae	No change
Balsami Tolu	No change
Aloes	No change
Gentianae	No change
Hydrastis	No change

TABLE II

RABBITS' WHOLE BLOOD *in vitro*

EXP. I

	Drug	*Clotting Time*
1.	NaCl 0.1 cc.	10 mins.
2.	Tr. Digitalis 0.1 cc.	5 mins.
3.	Tr. Cinchonae Comp. 0.1 cc.	8 mins.
4.	Tr. Lobeliae 0.1 cc.	9 mins.
5.	Tr. Nucis Vomicae 0.1 cc.	12 mins.
6.	Tr. Arnicae 0.1 cc.	13 mins.
7.	Tr. Hyoscyami 0.1 cc.	6 mins.
8.	Tr. Aconiti 0.1 cc.	6 mins.

EXP. II

1.	NaCl 0.2 cc.	11 mins.
2.	Tr. Opii 0.2 cc.	11 mins.
3.	Tr. Digitalis 0.2 cc.	6 mins.
4.	Tr. Strophanthi 0.2 cc.	6 mins.
5.	Tr. Hyoscyami 0.2 cc.	5 mins.
6.	Tr. Aconiti	5 mins.

EXP. III

1.	NaCl 0.2 cc.	7 mins.
2.	Tr. Nucis Vomicae 0.2 cc.	7 mins.
3.	Tr. Stramonii 0.2 cc.	5 mins.
4.	Tr. Belladonnae 0.2 cc.	4 mins.

TABLE III

CAT'S WHOLE BLOOD *in vitro*

Drug	*Clotting Time*
Physiological NaCl 0.2 cc.	9½ mins.
Tr. Cinchonae Comp. 0.2 cc.	9 mins.
Tr. Lobeliae 0.2 cc.	9½ mins.
Tr. Nucis Vomicae 0.2 cc.	9 mins.
Tr. Arnicae 0.2 cc.	30 mins.
Tr. Opii 0.2 cc.	4½ mins.
Tr. Hyoscyami 0.2 cc.	3 mins.
Tr. Belladonnae fol. 0.2 cc.	5 mins.

TABLE IV

HUMAN BLOOD (MR. J. K.) *in vitro*

Drug	*Clotting Time*
NaCl 0.2 cc.	11 mins.
Tr. Arnicae 0.2 cc.	25 mins.
Tr. Nucis Vomicae 0.2 cc.	10 mins.
Tr. Digitalis 0.2 cc.	8 mins.
Tr. Strophanthi 0.2 cc.	7½ mins.
Tr. Hyoscyami 0.2 cc.	7 mins.
Tr. Belladonnae 0.2 cc.	5½ mins.
Tr. Aconiti 0.2 cc.	7 mins.

TABLE V

RABBITS' BLOOD AFTER DRUG INJECTIONS INTO EAR VEIN

EXP. I

Normal Coagulation Time	11 mins.
1 hr. after 0.25 cc. Tr. Gentianae	11 mins.

EXP. II

Normal Coagulation Time	11 mins.
1 hr. after injection of 0.25 cc. Tr. Opii	4 mins.

EXP. III

Normal Coagulation Time	10 mins.
1 hr. after injection 0.25 cc. Tr. Hyoscyami	1 min.
3 hrs. after injection 0.25 cc. Tr. Hyoscyami	45 sec.

EXP. IV

Normal Coagulation Time	6½ mins.
1 hr. after injection 0.25 cc. Tr. Belladonnae	2 mins.
3 hrs. after injection 0.25 cc. Tr. Belladonnae	1 min.

TABLE VI

Rabbit Experiments by Stomach

Experiment 1: Rabbit 1800 Gms.

9.50 A. M.	Normal Coagulation Time	8	mins.
9.53 A. M.	Given by stomach tube 1 cc. Tr. Hyoscyami in water		
11.40 A. M.	Coagulation Time	45	secs.
2.10 P. M.	Coagulation Time	4	mins.

Experiment 2: Rabbit 1600 Gms.

10.05 A. M.	Normal Coagulation Time	6	mins.
10.08 A. M.	Given by stomach tube 1 cc. Tr. Belladonnae		
10.45 A. M.	Coagulation Time	1	min.
2.15 P. M.	Coagulation Time	2	mins.

Experiment 3: Rabbit 1200 Gms.

11.50 A. M.	Normal Coagulation Time	6	mins.
11.52 A. M.	Given by stomach tube 2 cc. Tr. Arnicae		
1.05 P. M.	Coagulation Time	6	mins.
2.20 P. M.	Coagulation Time	6	mins.

Experiment 4: Rabbit 1800 Gms.

10.23 A. M.	Normal Coagulation Time	5	mins.
10.25 A. M.	Given by stomach tube 1 cc. Tr. Aconiti		
11.30 A. M.	Coagulation Time	2	mins.
1.45 P. M.	Coagulation Time	1½	mins.

Experiment 5: Rabbit 1700 Gms.

10.30 A. M.	Normal Coagulation Time	6½	mins.
10.33 A. M.	Given by stomach tube 1 cc. Tr. Cinchonae Comp.		
11.35 A. M.	Coagulation Time	6½	mins.
1.50 P. M.	Coagulation Time	6½	mins.

Experiment 6: Rabbit 1200 Gms.

10.35 A. M.	Normal Coagulation Time	6	mins.
10.38 A. M.	Given by stomach tube 0.5 cc. Tr. Nucis Vomicae		
11.40 A. M.	Coagulation Time	6	mins.
1.55 P. M.	Coagulation Time	6	mins.

Experiment 7: Rabbit 1500 Gms.

10.48 A. M.	Normal Coagulation Time	5	mins.
10.50 A. M.	Given by stomach tube 1 cc. Tr. Hyoscyami		
11.50 A. M.	Coagulation Time	2	mins.
2.00 P. M.	Coagulation Time	1	min.

Experiment 8: Rabbit 1800 Gms.

9.55 A. M.	Normal Coagulation Time	6½	mins.
10.08 A. M.	Given by stomach tube 1 cc. Tr. Opii		
11.33 A. M.	Coagulation Time	2	mins.
1.30 P. M.	Coagulation Time	2	mins.

Experiment 9: Rabbit 1200 Gms.

10.23 A. M.	Normal Coagulation Time	5	mins.
10.26 A. M.	Given by stomach tube 1 cc. Tr. Valerianae		
11.37 A. M.	Coagulation Time	5	mins.

Experiment 10: Rabbit 1200 Gms.

10.30 A. M.	Normal Coagulation Time	5	mins.
10.33 A. M.	Given by stomach tube 1 cc. Fluidextr. Gentianae diluted with water		
11.45 A. M.	Coagulation Time	5	mins.

TABLE VII

RABBIT EXPERIMENTS WITH SOME ALKALOIDS INJECTED PARENTERALLY

Drug	*Coagulation Time*
Experiment 1: Rabbit 1800 Gms.	
Normal Coagulation Time	6 mins.
Injected Coniine HCl in vein, 2 mgs.	
1 hour later, coagulation time	3 mins.
3½ hours later	45 secs.
Experiment 2: Rabbit 1800 Gms.	
Normal Coagulation Time	5 mins.
Injected Hyoscyamine HCl, in vein, 2 mgs.	
1 hour later, coagulation time	2 mins.
3½ hours later	2½ mins.
Experiment 3: Rabbit 1500 Gms.	
Normal Coagulation Time	6½ mins.
Injected Scopolamine HBr in vein, 2 mgs.	
1 hour later, coagulation time	5½ mins.
3½ hours later	3 mins.
Experiment 4: Rabbit 1600 Gms.	
Normal Coagulation Time	6 mins.
Injected Gelsemine HCl in vein, 2 mgs.	
1 hour later, coagulation time	5 mins.
3½ hours later	6 mins.
Experiment 5: Rabbit 1200 Gms.	
Normal Coagulation Time	8 mins.
Injected in muscle, Morphine Sulf. 5 mgs.	
45 mins. later, coagulation time	2½ mins.
3 hours later	2 mins.
4½ hours later	1 min.

TABLE VIII

Repeated Blood Tests

Experiment 1: Large White Rabbit 2000 Gms.

June 24, 1948			
9.50 A. M.	Normal Coagulation Time	5½	mins.
10.35 A. M.	Normal Coagulation Time	7	mins.
11.35 A. M.	Normal Coagulation Time	6½	mins.
11.40 A. M.	Given by stomach tube, 1 cc. Tr. Opii		
2.00 P. M.	Coagulation Time	1	min.
June 25, 1948			
10.15 A. M.	Coagulation Time	5½	mins.

Experiment 2: Large Grey Rabbit 2000 Gms.

June 24, 1948			
10.00 A. M.	Normal Coagulation Time	14	mins.
11.00 A. M.	Normal Coagulation Time	14	mins.
11.50 A. M.	Normal Coagulation Time	15	mins.
11.55 A. M.	Given by stomach tube 1 cc. Tr. Hyoscyami		
2.15 P. M.	Coagulation Time	3	mins.
June 25, 1948			
10.20 A. M.	Coagulation Time	21	mins.

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SELECTED ABSTRACTS

The Value of Protein Hydrolysate in the Treatment of Peptic Ulcer—E. E. Woldman, D. Fishman, R. S. Knowlton, A. A. Rousuck and W. C. Stoner. *J. A. M. A. 137*:1289 (1948). None of the 22 patients with peptic ulcer who were included in the study reported gave evidence of protein deficiency. Consequently, if the patient is receiving a well balanced diet additional proteins will not aid in the healing of a peptic ulcer from a dietary standpoint.

The authors centered their attention on the value of protein hydrolysate as a buffering agent in the stomach. They found that a single dose of protein hydrolysate caused an increase in the total acid of the stomach but a decrease in the free acid value. The period of neutralization of free acid continues as long as the protein is in the stomach. Therefore, the longer the emptying time of the stomach or the larger the dose, the longer the period of neutralization. However, there is a sharp rise in the free acidity of the stomach after the amino acids enter the small intestine, and this acidity reaches a higher level than the initial level during the fasting state. Apparently the presence of the amino acids in the upper part of the small intestine stimulates the production of a hormone which in turn stimulates the production of hydrochloric acid in the stomach. It was also found that repeated small doses, such as by continuous drip with protein hydrolysate or hourly doses of 25 Gm., will eventually cease to neutralize the acid in the stomach. Evidently the presence of amino acids in the intestine stimulates hydrochloric acid production faster than subsequent small doses can buffer it.

Ulcer pain did not cease for 24 to 72 hours while patients were being treated with protein hydrolysate. In therapy with aluminum hydroxide gel the pain disappeared immediately. Pain also sometimes recurred during the course of treatment. There was recurrence of peptic ulcer symptoms in 8 of the 22 patients within a month after treatment was discontinued. Thus, the authors conclude that protein hydrolysate has little therapeutic value in the treatment of peptic ulcer.

Pharmacology and Chemotherapy of Sulphetrone—G. Brownlee, A. F. Green, and M. Woodbine. *Brit. J. Pharmacol. 3*:15 (1948). On the basis of experiments with mice and dogs it was concluded that Sulphetrone (4,4′-bis (γ-phenyl-n-propylamino) diphenylsulfone tetrasodium sulfonate) is practically non-toxic when given over short periods of time. The chronic toxicity, as studied in rabbits, was found to be low.

The drug is absorbed rather slowly, primarily through the small intestines. There is no evidence that it is conjugated in the intestinal tract. There is rapid penetration of all tissues with the exception of the brain. Penetration into the cerebrospinal fluid is not so rapid as with the other sulfonamides. There is no action on the heart, smooth muscle, nor on the blood pressure or respiration.

In vitro studies indicate that Sulphetrone is active against at least three strains of *Mycobacterium tuberculosis hominis* as well as several non-human strains. The presence of blood did not prevent this antibacterial activity. It was also found that the drug is effective against *beta*-hemolytic streptococcus infections in mice but that it is not effective against pneumococcus infections. The authors feel that the experimental results strongly suggest that Sulphetrone may prove effective in the treatment of tuberculosis experimentally in animals and possibly clinically in man.

Choloromycetin in the Treatment of Scrub Typhus—J. E. Smadel, T. E. Woodward, H. L. Ley, Jr., C. B. Philip, R. Traub, R. Lewthwaite and S. R. Savoor. *Science 108*:160 (1948). The antibiotic chloromycetin has been shown to have a beneficial therapeutic effect when administered experimentally to mice or in embryonated eggs which had been infected with a number of rickettsial agents. No toxic effects attributable to the antibiotic had been observed experimentally nor in a few patients in whom it was given clinical trial.

The authors report a series of 25 persons with proven scrub typhus who were treated with the drug and a control series of 12 untreated patients. The disease was proven by the isolation of *Rickettsia tsutsugamushi* from the blood prior to therapy or by demonstrating the development during convalescence of agglutinins for the OX-K strain of *B. proteus*. Twenty-two of the treated pa-

tients and 11 of the controls received their infections within a 20 mile radius of Kuala Lumpur, Malaya, and so the strains infecting the two groups were felt to be comparable in virulence.

Each patient in the treated group received an initial oral dose of 50 mg. of chloromycetin per Kg. of body weight with doses of 200 to 300 mg. every 2 to 4 hours thereafter. Treatment was continued until at least the 12th day following the onset of the disease. A gradual diminution of the time of therapy was followed until the last 7 cases received the drug for only 24 hours, with a total of about 6 Gm. being administered. The response with the short regime was as satisfactory as that with the longer periods.

In the treated group the fever was reduced to normal in an average of 31 hours after therapy was instituted with an average of 7.5 febrile days after onset of the disease. In the untreated group there were an average of 18.1 febrile days of illness. The treated patients were discharged from the hospital in an average of 19.2 days as compared with 30.7 days for the untreated patients. One death occurred in the untreated group but none among the treated patients.

Phenosulfazole Found to Halt Poliomyelitis in Mice—Report of work of M. E. Hultquist, R. Parker, and associates. *Chem. and Eng. News* 26:2710 (1948). A new synthetic sulfonamide compound, chemically *n*-(2-thiazolyl)-phenolsulfonamide, known informally as phenosulfazole, has been shown to be effective against mouse poliomyelitis. The drug has produced three types of results: mice were cured in the early stages of development of the disease, immunity was produced in those that survived, and single doses orally prevented infection.

The sodium salt of the drug is used to increase absorption. Mice were protected against as much as 100 times the lethal dose of poliomyelitis virus even when the sulfonamide was given 24 hours after the virus was administered. Mice in the control group all died from much smaller doses of the virus. The drug apparently acts on the tissue cell itself rather than directly on the virus. When the virus was placed in a cell-free serum containing the drug, the virus deteriorated at its normal unaffected rate. However, when the drug was added to embryonic mouse brain cultures infected with the virus

the growth of the virus halted abruptly. There seems to be no toxicity from the drug toward mice or monkeys.

Preliminary studies on the use of phenosulfazole in human beings has been started but no premature claims for a cure for human poliomyelitis is justified.

Studies of the Topical Application of Sodium Fluoride and Calcium Chloride in the Prophylaxis of Dental Caries—D. J. Galagan and J. W. Knutson. *Pub. Health Reports 63:*1215 (1948). The authors report the results of investigations of the effect on dental caries of the application of a 2 per cent solution of sodium fluoride, followed immediately by a 5 per cent solution of calcium chloride. It had been assumed that there would be a deposition of calcium fluoride on the tooth surface, and particularly in the enamel lamellae, which would further protect the tooth against caries. At the conclusion of the study it was concluded that calcium chloride does not increase caries inhibition over that of sodium fluoride alone.

In another phase of the study an effort was made to ascertain the effect of increased time intervals between applications of the 2 per cent solution of sodium fluoride. One series of patients was given the usual 4 applications at the rate of 1 or 2 treatments a week preceded by one cleansing. Another series was given 3 treatments at 3 month intervals, each treatment preceded by a cleansing of the teeth. Still another series received two treatments, each preceded by a cleansing, at intervals of six months. These longer time intervals decreased the caries-inhibiting action. There also seems to be a necessity for at least four applications for full effectiveness from the sodium fluoride solution.

A one per cent solution of sodium fluoride seems to be as effective as the usual 2 per cent solution, according to the results obtained with another series of patients. There was a reduction of 39 per cent in newly carious teeth as compared with opposite quadrants, untreated, in the same mouths. Four treatments were given to effect this reduction. Four treatments using a 2 per cent solution along with the calcium chloride effected a reduction of 32 per cent.

The authors also found that treatments were as effective whether applied by the usual cotton applicator or by means of a fine spray.

Stability of Penicillin Lozenges—N. H. Barnard and F. Hartley. *Pharm. J. 161*:160 (1948). The fact that the British Pharmacopoeia did not give any indication of the length of time of storage under prescribed conditions prompted the authors to present the results of their experiments on the storage stability of penicillin lozenges.

The lozenges were obtained from routine manufacture batches and stored in closed screw-capped jars with waxed board-lined caps. Storage was at room temperature. The base used was composed of equal parts of lactose and sucrose with sufficient powdered tragacanth. For granulation, mucilage of tragacanth was added. The calcium penicillin was dispersed in sterile magnesium stearate and added to the dry granules. Additional magnesium stearate was used for lubrication. Each finished lozenge weighed 1 Gm. and contained either 500 or 1000 units of penicillin.

The lozenges were assayed at intervals up to about one year. There was no significant loss of activity after a little more than a year, when assayed by the cup-plate method. The authors describe a special technique used in the preparation of the solution for assay.

In the discussion, reference was made to the penicillin tablet containers on the market containing silica gel and anhydrous cobalt chloride. The cobalt chloride is supposed to indicate when the danger point of moisture absorption has been passed by a change in color. The authors point out that this gives a sense of false security since the penicillin tablets may be used when they have actually absorbed sufficient moisture to have deteriorated. They point out that they had added water to such a container, the tablets absorbed the moisture, but there was still no change at all in the cobalt chloride.

BOOK REVIEW

Drug Research and Development—Edited by Austin Smith and Arthur D. Herrick. 596 pages incl. index; Revere Publishing Co., New York; 1948.

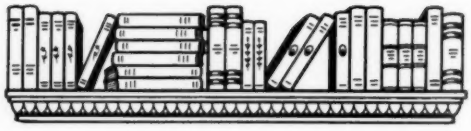
The editors, Dr. Smith and Mr. Herrick, are but two of the eighteen specialists who were the authors of this unusual book. It consists of a compilation of twenty-one chapters, each being a thorough treatment and discussion of some phase of the modern complicated process of evolving a new drug. Possibly no better means could be used to convey its scope and authoritative nature than to name its chapters and the author or authors who prepared each. They are as follows:

The Modern Drug Formula, by Arthur D. Herrick and Austin Smith;
Chemistry of the Formula, by Amel R. Menotti;
Pharmacology of the Formula, by Harvey B. Haag;
Laboratory Research, by M. L. Tainter;
Development of Biologicals, by Charles R. Linegar;
Clinical Testing, by Windsor C. Cutting;
Development of Facilities and Controls, by Edgar B. Carter;
Labels and Labeling, by John G. Searle;
Packaging and Storage, by R. H. Rhodehamel;
The Product and the Patent Law, by Edward Thomas;
Drug Trade-Marks and Labels, by Walter J. Derenberg;
Drug Regulation, by Arthur D. Herrick;
New Drug Applications, by Walton Van Winkle, Jr.;
Biologic Control Regulations, by Walter E. Ward;
Drug Certification, by Walton Van Winkle, Jr.;
Council Acceptance, by Austin Smith;
Product Development, Promotion and Marketing, by Robert A. Hardt;
Advertising, by Charles S. Downs;
"Detailing" the Physician, by Thomas H. Jones;
Professional Acceptance, by Austin Smith;
Retail Price Maintenance, by Isaac W. Digges.

Not only is the book of value to those who are engaged in pharmaceutical research and development but it also should prove most useful reading for all those who are engaged in the pharmaceutical field of endeavor. A broad understanding of the problems and requirements of all workers in this field is essential even for the specialist if his work is to become integrated in the overall picture.

The book is well conceived and it should enjoy widespread popularity and reading in the field of pharmacy.

L. F. Tice.



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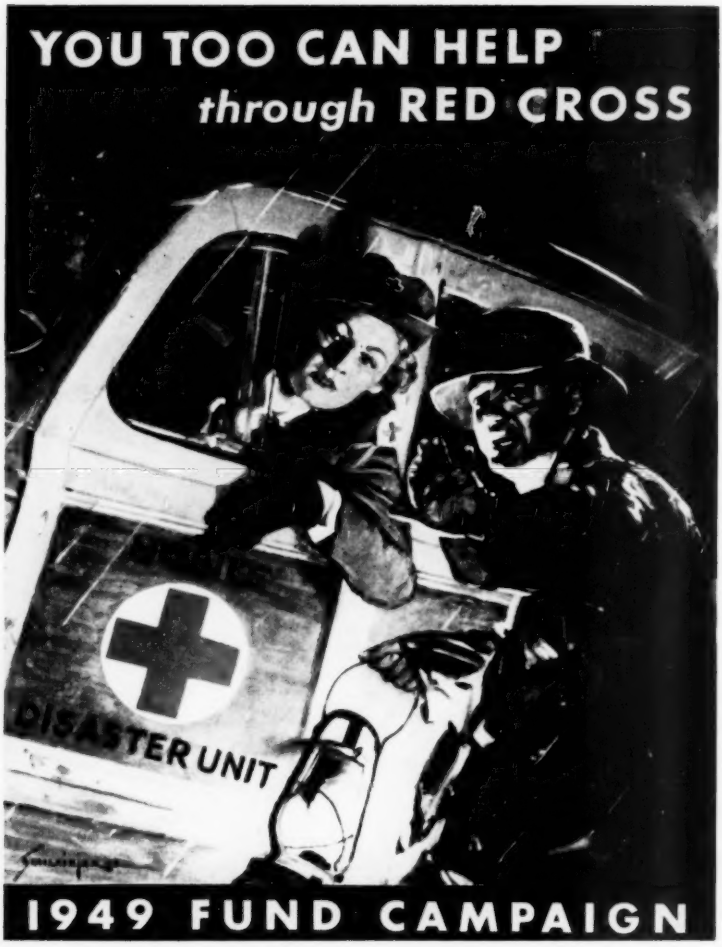
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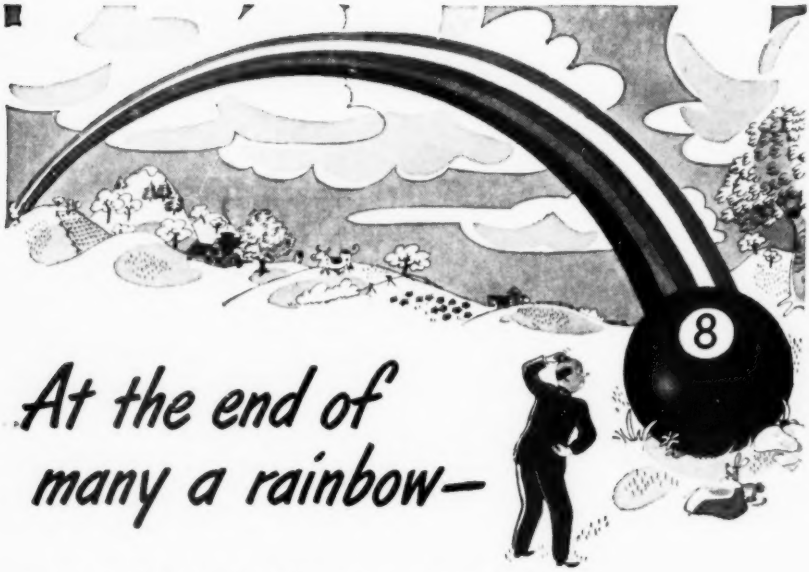

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